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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,481	11/29/2006	Stan Kubow	MGU0036US.NP	1887

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LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
CARTER, KENDRA D	
ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	10/591,481	KUBOW ET AL.	
	Examiner	Art Unit	
	KENDRA D. CARTER	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) *2,4 and 5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/3/08;11/29/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1 and 3, and fenretinide as the species in the reply filed on August 7, 2009 is acknowledged. The traversal is on the ground(s) that the Examiner has not shown anticipation of the claims. Particularly, the compound of Maurer et al. does not increase ceramide levels in cells of the respiratory tract. This is not found persuasive because the Examiner has established "an agent that increases ceramide levels in a cell" to be the special technical feature throughout the claims. Claim 3 does not require that the cells be from the respiratory tract.

An international application should relate to only one invention or, if there is more than one invention, the inclusion of those inventions in one international application is only permitted if all inventions are so linked as to form a single general inventive concept (PCT Rule 13.1). With respect to a group of inventions claimed in an international application, unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features.

The expression "special technical features" is defined in PCT Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. The determination is made on the contents of the claims as interpreted in light of the description and drawings (if any). Whether or not any particular technical feature makes a "contribution" over the prior art, and therefore constitutes a "special technical feature," should be considered with respect to novelty and inventive step.

As a result, no special technical features exist among the inventions because Maurer et al. teaches a compound that increases ceramide levels in a cell.

The Applicant has noted that Group IV should be claim 5 and not claim 4. The Examiner agrees and thus the restriction requirement should be corrected such that Group IV encompasses claim 5 and not claim 4.

Claims 2, 4 and 5 are withdrawn.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1) Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing a pro-inflammatory response in a diseased cell of the respiratory tract comprising contacting the cell with fenretinide, does not reasonably provide enablement for any agent that increases ceramide levels in any diseased cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method for inhibiting or reducing a pro-inflammatory response in a diseased cell of the respiratory tract comprising contacting a diseased cell of the respiratory tract with an agent that increases ceramide levels in the cell. The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art;

(6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 1 is drawn to "a method for inhibiting or reducing a pro-inflammatory response in a diseased cell of the respiratory tract comprising contacting a diseased cell of the respiratory tract with an agent that increases ceramide levels in the cell thereby inhibiting or reducing a pro-inflammatory response in the cell."

(2) The breadth of the claims:

Claim 1 embraces and reads on inhibiting or reducing a pro-inflammatory response in any diseased cell of the respiratory tract with any agent that increases ceramide levels. The specification does not enable the inhibition or reduction of a pro-inflammatory response in any diseased cell with any agent that increases ceramide levels.

(3) The state of the prior art:

The state of the art regarding effectively inhibiting or reducing a pro-inflammatory response in any diseased cell of the respiratory tract with any agent that increases ceramide levels is low or does not exist. Meacci et al. (Biochemical and Biophysical Research Communications, 1996, vol. 221, pp. 1-7) teach that the pro-inflammatory peptide bradykinin increases ceramide (see title and abstract), but there is no teaching

that bradykinin will inhibit or reduce the pro-inflammatory response in any diseased cell of the respiratory tract.

(4) The predictability or unpredictability of the art:

The predictability of inhibiting or reducing a pro-inflammatory response in any diseased cell of the respiratory tract with any agent that increases ceramide levels is relatively low, and therefore is unpredictable. In other words, just because there are potential therapeutic targets in by increasing ceramide levels, effective treatment or inhibition of pro-inflammatory response in a diseased cell of the respiratory tract has yet to be completely established. Therefore, because there is a "potential", inhibiting or reducing a pro-inflammatory response in any diseased cell of the respiratory tract with any agent that increases ceramide levels is unpredictable.

(5) The relative skill of those in the art:

The relative skill in the art is fairly high, with the typical practitioner having a medical degree and/or an advanced degree in the biochemical, chemistry or pharmaceutical-related arts, as evidenced by Maecci et al. and Maurer et al. (of record).

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to inhibiting or reducing a pro-inflammatory response in any diseased cell of the respiratory tract with any agent that increases ceramide levels is completely lacking. The specification as filed does not

speak on or show any working examples any studies performed that inhibit or reduce a pro-inflammatory response in any diseased cell of the respiratory tract with any agent that increases ceramide levels. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02. Particularly, the specification teaches that fenretinide can reduce the inflammatory immune hyper-responsiveness generated by the exaggerated activation of pro-inflammatory NF-kB in CFTR-deficient lug epithelial cells (see page 8, lines 24-32; and figure 5).

(7) The quantity of experimentation necessary:

The instant claims read on inhibiting or reducing a pro-inflammatory response in any diseased cell of the respiratory tract with any agent that increases ceramide levels. As discussed above the specification fails to provide any support for inhibiting or reducing a pro-inflammatory response in any diseased cell of the respiratory tract with any agent that increases ceramide levels. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation.

Particularly, the skilled practitioner would have to test each and every one of compounds as claimed, or at least a subset that is sufficiently representative of the compounds, to determine treatment efficacy for each condition. For example, to test for each disease of the respiratory tract, a particular compound that increases ceramide levels, would have to be selected, and a suitable test model and cell line would also

have to be selected. Some compounds might inhibit different pro-inflammatory responses that may require different test methods. If inhibition or reduction of the drug did not result, the amounts would have to be varied, or the test model may need to be changed to look for a different type of pro-inflammatory response (i.e. cytokine). If inhibition of a pro-inflammatory response of the condition was shown with the particular compound, then another compound that increases ceramide levels would have to be selected and the process would have to be repeated, including determining the optimum testing conditions. Thus, the skilled artisan would have to undergo exhaustive studies to evaluate each compound that increases ceramide levels for inhibiting or reducing a pro-inflammatory repsonse, in order to be able to fully carry out the invention commensurate in scope with the claims.

Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for reducing a pro-inflammatory response in a diseased cell of the respiratory tract comprising contacting the cell with fenretinide, but not for any agent that increases ceramide levels in any diseased cell of the respiratory tract.

2) Claim 3 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing an inflammatory response in respiratory tract cells comprising contacting a cell with fenretinide, does not reasonably provide enablement for any agent that increases ceramide levels to induce an inflammatory response in any cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method for inhibiting or reducing a pro-inflammatory response in a diseased cell of the respiratory tract comprising contacting a diseased cell of the respiratory tract with an agent that increases ceramide levels in the cell. The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 3 is drawn to "a method for inducing an inflammatory response in a cell comprising contacting a cell with an effective amount of an agent that increases the levels of ceramide in the cell thereby inducing an inflammatory response in the cell."

(2) The breadth of the claims:

Claim 3 embraces and reads on inducing an inflammatory response in any cell with any agent that increases the levels of ceramide. The specification does not enable inducing an inflammatory response in any cell with any agent that increases the levels of ceramide.

(3) The state of the prior art:

The state of the art regarding on inducing an inflammatory response in any cell with any agent that increases the levels of ceramide is low or does not exist. Meacci et al. (Biochemical and Biophysical Research Communications, 1996, vol. 221, pp. 1-7) teach that the pro-inflammatory peptide bradykinin increases ceramide (see title and abstract), but there is no teaching that bradykinin will induce an inflammatory response in any cell.

(4) The predictability or unpredictability of the art:

The predictability of on inducing an inflammatory response in any cell with any agent that increases the levels of ceramide is relatively low, and therefore is

unpredictable. In other words, just because there are potential agents to induce an inflammatory response by increasing ceramide levels, effective induction of an inflammatory response in a cell has yet to be completely established. Therefore, because there is a "potential", on inducing an inflammatory response in any cell with any agent that increases the levels of ceramide is unpredictable.

(5) The relative skill of those in the art:

The relative skill in the art is fairly high, with the typical practitioner having a medical degree and/or an advanced degree in the biochemical, chemistry or pharmaceutical-related arts, as evidenced by Maecci et al. and Maurer et al. (of record).

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to on inducing an inflammatory response in any cell with any agent that increases the levels of ceramide is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that on inducing an inflammatory response in any cell with any agent that increases the levels of ceramide. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02. Particularly, the specification teaches that fenretinide IL-8 concentrations in normal lug epithelial cells in the pro-inflammatory state were inhanced by fenretinide (see page 8, lines 24-29; and Figure 2)

(7) The quantity of experimentation necessary:

The instant claims read on inducing an inflammatory response in any cell with any agent that increases the levels of ceramide. As discussed above the specification fails to provide any support on inducing an inflammatory response in any cell with any agent that increases the levels of ceramide. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation.

Particularly, the skilled practitioner would have to test each and every one of compounds as claimed, or at least a subset that is sufficiently representative of the compounds, to determine induction for several normal cell lines. For example, to test for type of cell, a particular compound that increases ceramide levels, would have to be selected, and a suitable test model and cell line would also have to be selected. Some compounds might induce different inflammatory responses that may require different test methods. If induction of an inflammatory response with the drug did not result, the amounts would have to be varied, or the test model may need to be changed to look for a different type inflammatory response (i.e. cytokine). If induction of an inflammatory response was shown with the particular compound, then another compound that increases ceramide levels would have to be selected and the process would have to be repeated, including determining the optimum testing conditions. Thus, the skilled artisan would have to undergo exhaustive studies to evaluate each compound that increases ceramide levels for inducing an inflammatory response, in order to be able to

fully carry out the invention commensurate in scope with the claims.

Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for induction a pro-inflammatory response in a cell of the respiratory tract comprising contacting the cell with fenretinide, but not for any agent that increases ceramide levels in any cell.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1) Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dahl et al. (US 2003/0216471 A1).

Dahl et al. teach that treatment of diseases of the aerodigestive tract such as emphysema, COPD and inflammation (see abstract and column 48) with retinoids such as fenretinide (see paragraph 46). MCF-7 cells were contacted with the retinoid (see paragraph 54).

Dahl et al. does not teach that fenretinide specifically inhibits pro-inflammatory response in the diseased cell.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to use fenretinide to specifically reduce a pro-inflammatory response in a diseased cell of the respiratory tract because Dahl et al. teaches that retinoids including fenretinide treat respiratory diseases and inflammation upon contact. Thus, upon application of fenretinide to the respiratory tissue, the inflammation will be treated. In other words, it is obvious that the inflammatory response in the inflamed cells will be inhibited or reduced in order to be treated. The property of increasing ceramide levels is an inherent property of the compound. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case or either anticipation or obviousness has been established. Thus, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

2) Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mathias et al. (Biochem J., 1998, vol. 335, pp. 465-480) in view of Maurer et al. (Journal of the National Cancer Institute, 1999, vol. 91, no. 13, pp. 1138-146).

Mathias et al. teach the signal transduction of stress via ceramide (see title). Particularly, in macrophage cells ceramide causes inflammation (see page 469, table 1, line 4). Further, ceramide signals inflammation via the MAPK pathway (see page 472, column 1, last 3 lines).

Mathias et al. does not teach that fenretinide specifically induces the inflammatory response.

Maurer et al. teach that fenretinide increases ceramide in neuroblastoma cell lines (see title and abstract).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to use fenretinide to specifically induce an inflammatory response in a cell because fenretinide increases ceramide in cells as taught by Maurier et al. and ceramide induces inflammation as taught by Mathias et al.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kendra D Carter/
Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617